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EXAMINER	
BOESEN, AGNIESZKA	

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1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,644	SUNG ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-17 and 19-37* is/are pending in the application.

4a) Of the above claim(s) *30-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-17 and 19-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/18/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received April 12, 2007.

Election/Restrictions

Applicant's election with traverse of group I, claims 1-22 and 30-33 is acknowledged. In the telephonic interview with Applicant's representatives Laurence Manber and Hyun Soon Cho on April 24, 2007, Examiner informed Applicant's representatives that claims 30-33 have been inadvertently included together with linking claims 1-6, and 15-22 in the restriction requirement of February 13, 2007. This occurred because of the confounding recitation of the claimed method such as "a vaccine administrating method". Thus because claims 30-33 are method claims and the elected claims 1-22 are product claims, claims 30-33 are currently withdrawn because the claims are drawn to an invention that is distinct from the invention of claims 1-22. Upon further consideration claims 23-29 are rejoined.

With respect to the traversal of the restriction requirement, Applicants argue that the reference by Saito et al. does not disclose the limitations of the presently amended claims. It is noted that the reference by Saito et al. was cited because the reference teaches the special technical feature of the current invention, which is the recombinant adenovirus construct encoding HCV antigens. Thus because Saito et al. teach the special technical feature of the present invention, the claims are deemed to lack unity. Therefore the restriction is proper and is made FINAL.

Claims 30-37 are withdrawn because the claims are drawn to the non-elected invention.

Claims 3 and 18 are canceled. Claims 1, 2, 4-17, and 19-29 are under examination.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on March 18, 2005 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

Claim Objections

Claim 15 is objected to because of the following informalities: The claim recites "The DNA vaccine as set forth in claim 14, wherein the pGX10 hIL-12m is additionally contained." It is interpreted that the pGX10 hIL-12m is intended to be additionally contained within the claimed vaccine. However for the purpose of clarity Examiner suggests to rephrase the claim to recite "The DNA vaccine as set forth in claim 14, wherein the said vaccine further comprises the pGX10 hIL-12m."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-17, and 19-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is apparent that the plasmids: pGX10 gDsΔST (Accession No;

KCCM 10415), pGX10 NS34 (Accession No: KCCM 10417), and pGX10 NS5 (Accession NO; KCCM 10416); and adenoviruses: rAd gDsΔST (Accession No: KCCM 10418), rAd gDs NS34 (Accession No: KCCM 10420), and rAd gDs NS5 (Accession No: KCCM 10419) are required to practice the claimed invention. As such they must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise known and readily available to the public. It is noted that the Applicants have deposited the claimed plasmids and adenoviruses however there is no indication in the specification as to public availability.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

(a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years. Or 5 years after the last request for the enforceable life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit (see CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Claims 1, 2, 4-17, and 19-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make, and/or use the invention. The claims are drawn to a DNA vaccine and a recombinant adenovirus comprising a first plasmid containing a core gene, an E1 gene and E2 gene of HCV, a second plasmid containing an NS3 gene and an NS4 gene of HCV, and a third plasmid containing an NS5 gene of HCV.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, the factors deemed relevant are those of the amount of direction and the working examples provided, that quantity of experimentation necessary, the (un)predictability of the art, and the breadth of the claims.

The claims are rejected because the specification does not sufficiently support the claimed vaccines. The term "vaccine" by definition implies any preparation intended for active

immunological prophylaxis; e.g., preparations of killed microbes of virulent strains or living microbes of attenuated (variant or mutant) strains; or microbial, fungal, plant, protozoal, or metazoan derivatives or products. Although just about any protein when inoculated can cause an immune reaction, the prophylactic nature of this reaction is not guaranteed and has to be experimentally determined. Prophylaxis is defined as the prevention of disease or of a process that can lead to disease. This is achieved by use of an antigenic (immunogenic) agent to actively stimulate the immunological mechanism, or the administration of chemicals or drugs to members of a community to reduce the number of carriers of a disease and to prevent others contracting the disease. A vaccine composition can thus be interpreted to be a drug, which by definition is an agent intentioned for the use in the diagnostics, mitigation, treatment, cure, or prevention of disease in humans or in other animals. The current claims are drawn a vaccine comprising an HCV nucleic acid. Tang et al., (Recent advances in DNA vaccine of hepatitis virus, Hepatobiliary & Pancreatic Dis. Inter., 2002, Vol. 1, p. 228-231) discuses problems associated with DNA immunization and vaccination against HCV. Lechman et al. (Vaccine development for Hepatitis C, Seminars in Liver Diseases, 2000, Vol. 20, p. 211-226) teaches that because the HCV virus can mutate rapidly causing a high heterogeneity allowing the virus to evade the immune system of the host, the HCV causes persistent infection in the immune competent host despite active immune response. Despite numerous efforts of the scientists to generate protective HCV vaccine for human use, the effective HCV vaccine does not currently exist. One of the obstacles in HCV vaccine development is the lack of a small animal model and cell culture systems. Several vaccine candidates have been tested in chimpanzees, however those vaccine as of the present time, have not been shown to confer protection from HCV infection in humans

(see Mikkelsen and Bukh, Current status of hepatitis C vaccine: encouraging results but significant challenges ahead, Current Infectious Diseases Reports, Vol. 9, p. 94-101). Thus unless the efficacy of the claimed vaccine is tested in phase II clinical trials, one cannot determine if the claimed vaccine has any therapeutic effect.

The current specification does not set forth sufficient teachings to allow one skilled in the art to use the claimed vaccine or the immunogenic composition to prevent the HCV infection in humans. It is acknowledged that Applicants have provided evidenced that chimpanzees immunized with the presently claimed vaccine, and challenged with infectious hepatitis C have shown undetectable levels of the HCV virus in the blood (Example 16 and Figure 19 of the specification). It is also acknowledged that Applicants have provided evidence that the presently claimed vaccines are capable of inducing cellular immune responses when administered to mice and chimpanzees (Examples 1-15, and Figures 9-15). However, because an effective vaccine against HCV infection is not presently available, and because the effectiveness of HCV vaccine in chimpanzees has not been proven in humans, one would be unable to conclude that the presently claimed vaccines can be successfully used to prevent HCV infection in humans.

For the above reasons, it appears that undue experimentation would be required to practice the claimed invention with a reasonable expectation of success. In order to determine the efficacy of the claimed vaccines for human use, the skilled artisan would require to conduct clinical trials involving a representative human population. In the absence of data obtained from clinical trials testing the claimed vaccines, the present disclosure does not enable one skilled in the art to practice the claimed invention in its full scope.

Applicants have not provided any convincing evidence that their claimed vaccine is indeed useful as a therapeutic or preventative for HCV infection in humans and have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 6, 16, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Saito et al. (US Patent 5,731,172). Note that the claims are rejected for the recited components, not the non-enabled vaccine applications.

Claims are drawn to a DNA vaccine comprising a first plasmid containing a core gene, an E1 gene and E2 gene of HCV, a second plasmid containing an NS3 gene and an NS4 gene of HCV, and a third plasmid containing an NS5 gene of HCV. The claims are also drawn to a recombinant adenovirus vaccine comprising first plasmid containing a core gene, an E1 gene and E2 gene of HCV, a second plasmid containing an NS3 gene and an NS4 gene of HCV, and a

third plasmid containing an NS5 gene of HCV. The size of HCV genes contained in the first, second and third plasmid ranges from 2 to 4 kb. Because the claims recite an open language such as comprising and containing, the claims read on a vaccine comprising the whole genome of the HCV virus.

Saito et al. disclose a recombinant adenovirus vaccine comprising plasmids expressing the HCV genes (see Example 2). Although Saito et al. does not specifically disclose which HCV genes are expressed by the recombinant adenovirus, because Saito et al. broadly speaks about the whole HCV genome, it is expected that all HCV genes, including E1, E2, NS3, NS4, and NS5 are present in Saito's recombinant adenoviral vaccine. Thus by this disclosure Saito et al. anticipate the current claims.

Claims 1, 2, and 6 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al. (US 2004/0166488 A1).

Claims are drawn to a DNA vaccine comprising a first plasmid containing a core gene, an E1 gene and E2 gene of HCV, a second plasmid containing an NS3 gene and an NS4 gene of HCV, and a third plasmid containing an NS5 gene of HCV. The size of HCV genes contained in the first, second and third plasmid ranges from 2 to 4 kb. Because the claims recite an open language such as comprising and containing, the claims read on a vaccine comprising the whole genome of the HCV virus.

Tang et al. disclose a vaccine comprising a complete HCV genome comprising E1, E2, NS3, NS4, and NS5 genes of HCV (see [0007], [0024], [0034-0039], and claims 1-3). With regard to the limitations drawn to the size of the plasmids, the size of the particular genes comprised within the vaccine disclosed by Tang et al. is expected to range from 2 to 4 kb,

because the HCV genes of the current invention and HCV genes disclosed by Tang et al. have identical structure. Although some variations may exist in different strains of the HCV virus with respect to the particular nucleic acids and certain positions, the length and thus the size of the genes remain the same. Therefore Tang et al. anticipate the current invention.

Claims 1, 2, and 6 are rejected under 35 U.S.C. 102(a) as being anticipated by Pancholi et al. (Journal of Virology, January 2003, Vol. 77, p. 382-390). Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claims are drawn to a DNA vaccine comprising a first plasmid containing a core gene, an E1 gene and E2 gene of HCV, a second plasmid containing an NS3 gene and an NS4 gene of HCV, and a third plasmid containing an NS5 gene of HCV. The size of HCV genes contained in the first, second and third plasmid ranges from 2 to 4 kb. Because the claims recite an open language such as comprising and containing, the claims read on a vaccine comprising the whole genome of the HCV virus.

Pancholi et al. disclose DNA vaccine comprising E1, E2, NS3, NS4, and NS5 genes of HCV delivered as a plasmid DNA (see the entire document, particularly page 382, and Materials and Methods). With regard to the limitations drawn to the size of the plasmids, the size of the particular genes comprised within the vaccine disclosed by Pancholi et al. is expected to range from 2 to 4 kb, because the HCV genes of the current invention and HCV genes disclosed by Pancholi et al. have identical structure. Although some variations may exist in different strains

of the HCV virus with respect to the particular nucleic acids and certain positions, the length and thus the size of the genes remains the same. Therefore Pancholi et al. anticipate the current invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AB

Agnieszka Boesen, Ph.D.

/Stacy B. Chen/ May 21, 2007
Primary Examiner, TC1600